## SEQUENCE LISTING

| sll. Perett F. Monia<br>Lex M. Cowsert<br>Sue Murray<br>Mandy Butler<br>Nock Dean  |     |
|--|-----|
| <120 > ANTISENSE MODULATION OF PIBK PES EXPRESSION   |     |
| <130> ISPH-0519  |     |
| <1608 M3   |     |
| <pre>&lt;210: 1 &lt;211% 3372 &lt;212: INA &lt;213: Homo sapiens</pre>   |     |
| <220:<br><221> CDS<br><222: 43)(2217)  |     |
| <pre>c400% 1 tacaaccagg ctraartgtt geatggtage agatttgcaa ac atg agt get gag</pre>  | 54  |
| ggg tac dag tad aga gog dtg tat gat tat aaa aag gaa aga gaa gaa<br>Gly Tyr Gln Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys Glu Arg Glu Glu<br>5 10 20  | 102 |
| gat att gad tig bad tig ggt gad ata tig adt gig aat aaa ggg tod<br>Asp lle Asp Leu His Leu Gly Asp Ile Leu Thr Val Ash Lys Gly Ser<br>25 30 35 | 150 |
| tta gta got ott gga tto agt gat gga dag gaa god agg oot gaa gaa<br>Leu Val Ala Leu Gly Phe Ser Asp Gly Gln Glu Ala Arg Pro Glu Glu<br>40 45 50 | 198 |
| att ggc tgg tta aat ggc tat aat gaa acc aca ggg gaa agg ggg gac<br>Ile Gly Trp Leu Asn Gly Tyr Asn Glu Thr Thr Gly Glu Arg Gly Asp<br>55 60 65 | 246 |
| tit dog gga act tad gta gaa tat att gga agg aaa aaa atd tog dot<br>Phe Pro Gly Thr Tyr Val Glu Tyr Ile Gly Arg Lys Lys Ile Ser Pro<br>75 80    | 294 |
| pro Thr Pro Lys Pro Arg Pro Pro Arg Pro Leu Pro Val Ala Pro Gly 85 90 90   | 342 |
| tot tog aaa act gaa goa gat gtt gaa caa caa got ttg act oto dog<br>Ser Ser Lys Thr Glu Ala Asp Val Glu Gln Gln Ala Leu Thr Leu Pro<br>105 116  | 390 |
| gat our goa gag dag tit god oof oot gad att god dog oot out out  | 438 |

-

| Asp               | 14                                       | Ala               | 314<br>10.        | 31n               | Fi.e              | Ala                  | Pri               | Pro<br>125        | Asp               | 116               | Ala               | Pro               | F10               | Leu               | Leu               |        |
|-------------------|--|-------------------|-------------------|-------------------|-------------------|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------|
| :5:               | aag<br>Lys                               | 303<br>Leu<br>135 | 954<br>Val        | gaa<br>31u        | goo<br>Ala        | att                  | gaa<br>31u<br>141 | aag<br>Lys        | ada<br>Lys        | 955<br>955        | atg<br>Leu        | gaā<br>314<br>148 | tgt<br>Cys        | 103<br>Šež        | apt<br>Thr        | વે કહે |
| ēta<br>Leu        | ta:<br>Tiri                              | aga<br>Arg        | aba<br>Thr        | cag<br>Gln        | agc<br>Ser        | 50<br>50<br>55<br>15 | ago<br>Ser        | aac<br>Asn        | otg<br>Leu        | gca<br>Ala        | gaa<br>Glu<br>160 | tta<br>Leu        | oga<br>Arg        | cag<br>Gln        | ett<br>Leu        | 534    |
| att<br>Leu<br>165 | gat<br>Asp                               | tgt<br>Cys        | gat<br>Asp        | aca<br>Thr        | ccc<br>Pro<br>100 | too<br>Ser           | gtg<br>Val        | gac<br>Asp        | ttg<br>Leu        | gaa<br>Glu<br>175 | atg<br>Met        | atc<br>Ile        | gat<br>Asp        | gtg<br>Val        | cac<br>His<br>180 | 582    |
| gtt<br>Tal        | 5 J. | got<br>Ala        | gac<br>Asp        | gct<br>Ala<br>185 | ttc<br>Phe        | aaa<br>Lys           | Arg<br>oge        | tat<br>Tyr        | ata<br>180        | ctg<br>Leu        | gac<br>Asp        | tta<br>Leu        | cca<br>Pro        | aat<br>Asn<br>195 | oot<br>Pro        | 630    |
| gtc<br>Val        | att<br>Ilė                               | cca<br>Pro        | gca<br>Ala<br>200 | gcc<br>Ala        | gtt<br>Val        | tac<br>Tyr           | agt<br>Ser        | gaa<br>Glu<br>205 | atg<br>Met        | att<br>Ile        | tat<br>Ser        | tta<br>Leu        | get<br>Ala<br>210 | cca<br>Pro        | gaa<br>Glu        | 678    |
| gta<br>Val        | caa<br>Glr.                              | agc<br>Ser<br>215 | too<br>Ser        | gaa<br>Glu        | gaa<br>Glu        | tat<br>Tyr           | att<br>Ile<br>220 | cag<br>Gln        | cta<br>Leu        | ttg<br>Leu        | aag<br>Lys        | aag<br>Lys<br>225 | ott<br>Leu        | att<br>Ile        | agg<br>Arg        | 726    |
|                   |  |                   |                   |                   | cat<br>His        |                      |                   |                   |                   |                   |                   |                   |                   |                   |                   | 774    |
| aaa<br>Lys<br>245 | cat<br>His                               | t to<br>Pae       | tto<br>Phe        | aag<br>Lys        | ata<br>Leu<br>250 | tct<br>Ser           | caa<br>Gln        | acc<br>Thr        | too<br>Ser        | agc<br>Ser<br>255 | aaa<br>Lys        | aat<br>Asn        | otg<br>Leu        | ttg<br>Leu        | aat<br>Asn<br>260 | 822    |
| gca<br>Ala        | aga<br>Arg                               | gta<br>Val        | ata<br>Leu        | tot<br>Ser<br>265 | gaa<br>Glu        | att<br>Ile           | ttc<br>Phe        | agc<br>Ser        | dat<br>Pro<br>270 | atg<br>Met        | ctt<br>Leu        | tto<br>Phe        | aga<br>Arg        | ttc<br>Fhe<br>275 | tca<br>Ser        | 870    |
| gca<br>Ala        | gcc<br>Ala                               | agc<br>Ser        | tot<br>Ser<br>230 | gat<br>Asp        | aat<br>Asn        | act<br>Thr           | gaa<br>Glu        | aac<br>Asn<br>285 | ctc<br>Leu        | ata<br>Ile        | aaa<br>Lys        | gtt<br>Val        | ata<br>Ile<br>290 | gaa<br>Glu        | att<br>Ile        | 918    |
| tta<br>Leu        | atc<br>Ilé                               | toa<br>Ser<br>295 | act<br>Thr        | gaa<br>Glu        | tgg<br>Trp        | aat<br>Asn           | gaa<br>Glu<br>500 | cga<br>Arg        | cag<br>Gln        | aat<br>Pro        | gca<br>Ala        | cca<br>Pro<br>305 | gca<br>Ala        | ctg<br>Leu        | oct<br>Pro        | 966    |
| ost<br>Pro        | aa.<br>Lys<br>310                        | cca<br>Pro        | cca<br>Pro        | aaa<br>Lys        | cct<br>Pro        | ast<br>Thr<br>315    | act<br>Thr        | gta<br>Val        | gcc<br>Ala        | aac<br>Asn        | aac<br>Asn<br>320 | ggt<br>Gly        | atg<br>Met        | aat<br>Asn        | aac<br>Asn        | 1014   |
|                   |  |                   |                   |                   | aat<br>Asn<br>330 |                      |                   |                   |                   |                   |                   |                   |                   |                   |                   | 1062   |
| gaa<br>Glu        | gaa<br>31.                               | gtg<br>Val        | aat<br>Asn        | gaa<br>Glu<br>345 | aaa<br>Lys        | ott<br>Leu           | oga<br>Arg        | gat<br>Asp        | aca<br>Thr<br>33. | gca<br>Ala        | gac<br>Asp        | 317.<br>333       | acc<br>Thr        | 555<br>Fle        | ttg<br>Leu        | 1115   |

| gta ogu g<br>Val Arg A         | at gog :<br>sp Ala :      | tot act<br>Ser Thr        | aaa :<br>Lys :        | Mat                        | cat<br>His<br>365 | 995<br>917        | gat<br>Asp        | tat<br>Tyr        | apt<br>Thr        | 011<br>164<br>371 | aca<br>Thr        | ota<br>Leu             | 1058 |
|--------------------------------|---------------------------|---------------------------|-----------------------|----------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------------------------|------|
| agg aaa g<br>Ard Lyk 3<br>3    | gg gga<br>ly gly .<br>Th  | aat aat<br>Asn Asn        | Lys :                 | tta .<br>Leu :<br>380      | ato<br>Ile        | aaa<br>Lys        | ata<br>Ile        | ttt<br>Phe        | Cat<br>His<br>365 | oga<br>Arg        | gat<br>Asp        | 999<br>917             | 1208 |
| aaa tat g<br>Lys Tyr 3<br>390  | ga tta<br>ly Phē .        | tot gad<br>Ser Asp        | 00a :<br>Pro :<br>395 | tta :<br>Leu 1             | acc<br>Thr        | tto<br>Phe        | agt<br>Ser        | tot<br>Ser<br>ico | gtg<br>Val        | gtt<br>Val        | gaa<br>31u        | ttā<br>Leu             | 1254 |
| ata aac co<br>Ile Asm H<br>405 | ac tac<br>is Tyr .        | ogg aat<br>Arg Asn<br>410 | gaa :<br>Glu :        | tat :<br>Ser :             | cta<br>Leu        | gct<br>Ala        | cag<br>Gln<br>415 | tat<br>Tyr        | aat<br>Asn        | occ<br>Pro        | aaa<br>Lys        | ttg<br>1eu<br>420      | 1302 |
| gat gtg a<br>Asp Val L         | /s let                    | ott tat<br>Led Tyr<br>425 | oda ş<br>Pro          | gta :<br>Val :             | tos<br>Ser        | aaa<br>Lys<br>430 | tac<br>Tyr        | caa<br>Jln        | dag<br>Gln        | gat<br>Asp        | caa<br>31n<br>435 | gtt<br>Val             | 1350 |
| gtc aas g<br>Val Lys G         | aa gat<br>lu Asp .<br>440 | aat att<br>Asn Ile        | gaa q<br>Glu A        | Ala '                      | gta<br>Val<br>445 | 999<br>999        | aaa<br>Lys        | aaa<br>Lys        | tta<br>Leu        | cat<br>His<br>450 | gaa<br>Glu        | tat<br>Tyr             | 1398 |
| aac act c<br>Asn Thr G<br>4    | ag ttt<br>ln Phe<br>53    | caa gaa<br>Glu Glu        | Lys S                 | agt<br>Ser <i>1</i><br>460 | oga<br>Arg        | gaa<br>Glu        | tat<br>Tyr        | gat<br>Asp        | aga<br>Arg<br>465 | tta<br>Leu        | tat<br>Tyr        | gaa<br>Glu             | 1446 |
| gaa tat a<br>Glu Tyr Tl<br>470 | oc ogs<br>hr Arg          | ada tod<br>Thr Ser        | cag 9<br>Gln (<br>475 | gaa .<br>Glu               | atc<br>Ile        | caa<br>Gln        | atg<br>Met        | aaa<br>Lys<br>480 | agg<br>Arg        | aca<br>Thr        | gct<br>Ala        | att<br>Ile             | 1494 |
| gaa gca t<br>Glu Ala P<br>485  | tt aat<br>he Asn          | gaa acc<br>Glu Thr<br>490 | ata a<br>Ile :        | aaa<br>Lys                 | ata<br>Ile        | ttt<br>Phe        | gaa<br>Glu<br>495 | gaa<br>Glu        | cag<br>Gln        | tge<br>tge        | cag<br>Gln        | acc<br>Thr<br>500      | 1542 |
| caa gag c<br>Gln Glu A         | rg Tyr .                  | agd aaa<br>Ser Lys<br>505 | gaa 1<br>Glu 1        | tac .<br>Tyr               | ata<br>Ile        | gaa<br>Glu<br>510 | aag<br>Lys        | ttt<br>Phe        | aaa<br>Lys        | ogt<br>Arg        | gaa<br>Glu<br>515 | 61 <sup>7</sup><br>83c | 1590 |
| aat gag a<br>Asn Glu L         | aa gaa<br>ys Glu<br>520   | ata caa<br>Ile Gln        | agg (<br>Arg )        | ile :                      | atg<br>Met<br>525 | cat<br>His        | aat<br>Asn        | tat<br>Tyr        | gat.<br>Asp       | aag<br>Lys<br>530 | ttg<br>Leu        | aag<br>Lys             | 1638 |
| tot oga a<br>Ser Arg I<br>5    |                           |                           | Ile A                 |                            |                   |                   |                   |                   |                   |                   |                   |                        | 1686 |
| ttg aag a<br>Leu Lys Ly<br>550 | ag sag<br>ys Gln .        | gca got<br>Ala Ala        | gag :<br>Glu :<br>555 | tat<br>Tyr :               | oga<br>Arg        | gaa<br>Glu        | att<br>Ile        | gac<br>Asp<br>560 | aaa<br>Lys        | ogt<br>Arg        | atg<br>Met        | aac<br>Asn             | 1734 |
| ago att a<br>Ser Ile L<br>565  | aa cca<br>ys Pro .        | gad ott<br>Asp Leu<br>570 | ats (<br>ile (        | cag (<br>Gl:: )            | ctg<br>Leu        | aga<br>Arg        | aag<br>Lys<br>575 | acg<br>Tnr        | aga<br>Arg        | gac<br>Asp        | caa<br>Gln        | tac<br>Tyr<br>580      | 1782 |
| tig atg t:<br>Led Met T        | rp Leu '                  | act caa<br>Thr Gln<br>585 | aaa<br>Lys            | ggt (<br>Gly               | gtt<br>Val        | ess<br>Vra<br>caa | daa<br>Glm        | aag<br>Lys        | aag<br>Lys        | ttg<br>Leu        | aac<br>Asn<br>S98 | gag<br>Glu             | 1830 |

| tgg ttg ggo aat gaa aas ast gaa gas caa tat toa otg gtg gaa gat<br>Trp Lew Sly Asn Slu Asn Thr Slu Asp Gln Tyr Ser Leu Val Glu Asp<br>615 615  | 1878                 |
|--|----------------------|
| gat gak gat tig 600 cat dat gat gag aag aca igg aat git gga ago<br>Asp 31. Asp Leu Pro His His Asp 31u Lys Thr Try Ash Val 31y Ser<br>610 625  | 1926                 |
| ago aar oga aac aaa got gaa aac ptg ttg bga ggg aag oga gat ggc<br>Ser Asi Arg Asn Lys Ala 3lu Asn Leu Leu Arg 3ly Lys Arg Asp 3ly<br>63l 640  | 1974                 |
| act tit cit gic ogg gag ago agi aaa dag ggo igo iai god igo ici<br>Thr Phe Leu Val Arg Glu Ser Ser Lys Gln Gly Cys Tyr Ala Cys Ser<br>645 650 660  | 2022                 |
| gta gtg gtg gac ggc gaa gta aag cat tgt gtc ata aac aaa aca gca<br>Wal Val Asp Gly Glu Val Lys His Cys Val Ile Asn Lys Thr Ala<br>665 670 675  | 2070                 |
| act gg0 tat gg0 tit gc0 gag cc0 tat aac tig tad ag0 tot otg aaa<br>Thr Gly Tyr Gly Phe Ala Glu Pro Tyr Asn Leu Tyr Ser Ser Leu Lys<br>680 685 690  | 2118                 |
| gaa otg gtg ota oat tao oaa oac aco too ott gtg oag oac aac gac<br>Glu Leu Val Leu His Tyr Gln His Thr Ser Leu Val Gln His Asn Asp<br>695 700 705  | 1.166                |
| too oto aat gto aca ota goo tac oca gta tat goa cag cag agg oga<br>Ser Leu Asn Val Thr Leu Ala Tyr Pro Val Tyr Ala Gln Gln Arg Arg<br>710 715 720  | 2214                 |
| tga agegettast etttgatset tetestgaag ttsagsease stgaggeets<br>705  | 1.267                |
| tggaaagcaa agggeteete teragtetga tetgtgaatt gagetgeaga aabgaageea  | 2327                 |
| totttotttg gatgggasta gagstttott tsasaaaaaa gaagtagggg aagacatgca  | 1387                 |
| gootaaggot gtatgatgas sasasgttse taagstggag tgsttatess ttstttttt   | 2447                 |
| tttttttttttttt gytttaattt aaagodabaa obabatabaa dabaaagaga aaaagaaatg  | 2507                 |
| caaaaatoto tgogtgoagg gabaaagagg ootttaacca tggtgottgt taatgottto  | 2567                 |
| tgaagottta ccagotgaaa gttgggacto tggagagogg aggagagaga ggcagaagaa  | 4607                 |
| and added to an added to a second and the added to a second to a second to a   | 2627                 |
| occtggootg agaaggtotg gtocagootg gtttagootg gatgttgotg tgcaoggtgg  | 2687                 |
| acccagacae atogoactgt ggattattte attttgtaac aaatgaacga tatgtagcag  | 2687<br>2747         |
| accoagacac atogoactgt ggattatttc attttgtaac aaatgaacga tatgtagcag<br>aaaggcatgt ccactcacaa gggatgettt gggagaatgt cagttcatgt atgttcagaa   | 2687<br>2747<br>2807 |
| acccagacac atogoactgt ggattattte attitigtaac aaatgaacga tatgtagcag<br>aaaggcatgt ccactcacaa gggatgettt gggagaatgt cagttcatgt atgttcagaa<br>gaaattetgt catagaaagt gccagaaagt gtttaacttg tcaaaaaaca aaaacccagc | 2687<br>2747         |
| accoagacac atogoactgt ggattatttc attttgtaac aaatgaacga tatgtagcag<br>aaaggcatgt ccactcacaa gggatgettt gggagaatgt cagttcatgt atgttcagaa   | 2687<br>2747<br>2807 |

| tytittyitt tyytyääyyy tääättiava gugutatytä ättytt   | aatt disabtaagi (1847) |
|--|------------------------|
| tyttatttoa yttttaaaty täpottoaya ataagottoo obacco   | ougt ittigtight 3117   |
| tgäääätiatt gttgtooogg atttttgtta atattvättt ttgtta  | toot titttaaaaa 3167   |
| taaatgtaca ggatgocagt aaaaaaaaaa atggottoag aattaa   | aadt atgaaatatt 3007   |
| ttadagtttt tottgtadag ägtadttgdt gttagdddaa ggttaa   | aaag tibataadag 3087   |
| attrittitig gadigittitg tigggdagig oqtgataagd tidaad | gotg otttattoaa 3347   |
| taaaaaaaa aooogaatto aotgg                           | 3372                   |
|  |                        |
| <2109-2  |                        |
| <211: 21   |                        |
| ::210: ENA   |                        |
| :2135 Artificial Sequence                            |                        |
|  |                        |
| (223)  |                        |
| .223: FCR Primer                                     |                        |
|  |                        |
| 4400× 2  |                        |
| agcaacctgg cagaattacg a                              | 21                     |
|  |                        |
| <210× 3  |                        |
| :2115: 21  |                        |
| 3213> INA  |                        |
| <213> Artificial Sequence                            |                        |
| -  |                        |
| <220>  |                        |
| <221> PCR Primer                                     |                        |
|  |                        |
| -:400p 3   |                        |
| maaaacgugo acatogatoa t                              | 21                     |
|  |                        |
|  |                        |
| *210: 4  |                        |
| #211; 30   |                        |
| \$010x 0XA   |                        |

<2135 Artificial Sequence

| CLUT                                    |    |
|---|----|
| K223s ICR Probe                         |    |
|   |    |
|   |    |
|   |    |
| titottigatty tgatavavov tocgtygast      | 30 |
|   |    |
|   |    |
| KOION E                                 |    |
| 4211×19                                 |    |
|   |    |
| COIO: ENA                               |    |
| 4213: Artificial Sequence               |    |
|   |    |
| .220:                                   |    |
| t223% FCR Primer                        |    |
| ALLOW FOR FIRMOR                        |    |
|   |    |
| :400: E                                 |    |
| gaaggtgaag gtcggagtc                    | 19 |
|   |    |
|   |    |
| k210:- 6                                |    |
|   |    |
| :211:- 20                               |    |
| K2125 DNA                               |    |
| <pre>&lt;213: Artificial Sequence</pre> |    |
|   |    |
| x220x                                   |    |
| :223: PCR Primer                        |    |
| :223: PCR PITMET                        |    |
|   |    |
| :400: 6                                 |    |
| gaagatggtg atgggatttc                   | 20 |
|   |    |
|   |    |
| 010 5                                   |    |
| 4210) 7                                 |    |
| <211: CO                                |    |
| ₹210: UNA                               |    |
| -213- Artificial Sequence               |    |
|   |    |
| ROSTN                                   |    |
|   |    |

<223: FCR Probe

| kásco <sup>n</sup>   |    |
|--|----|
| daagnttodo gttotdagdo  | 20 |
|  |    |
|  |    |
| ROIDM B  |    |
| V211x 18   |    |
| 4010: DNA  |    |
| k213: Artificial Sequence  |    |
|  |    |
| 4223:  |    |
| (223): Antisense Oligonuoleotide   |    |
|  |    |
| 1400H B  |    |
| atetrettet etttett   | 18 |
|  |    |
|  |    |
| <210× 9  |    |
| <211× 18   |    |
| <212> DNA  |    |
| (213> Artificial Sequence  |    |
| All and a sequence   |    |
|  |    |
| RECENT Antisense Oligonucleotide   |    |
|  |    |
| < 400 × 19   |    |
| gotteetgte bateastg  | 18 |
|  |    |
|  |    |
| WG10.0 10  |    |
|  |    |
| <010 - 01A   |    |
| <pre></pre>  |    |
|  |    |
| ₹220:-   |    |
| <pre>&lt;223: Antisense Oligonucleotide</pre>  |    |
| .223   |    |
| K400 K 10  |    |
| The strength of the strength o | 19 |
| # 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0  |    |

| \$220                                      |    |
|--|----|
| (\$211): 18                                |    |
| CIC - INA                                  |    |
| .213 Artifibial Sequênde                   |    |
|  |    |
| w2201                                      |    |
| k223: Antisense Oligonuoleotide            |    |
|  |    |
| 8400x 11                                   |    |
| lattitgaca ggttgatg                        | 18 |
|  |    |
|  |    |
| .210: 12                                   |    |
| :211>-13                                   |    |
| :210: ENA                                  |    |
| <pre>&lt;213: Artificial Sequence</pre>    |    |
|  |    |
| k220:                                      |    |
| :223: Antisense Oligonucleotide            |    |
|  |    |
| :400:- 12                                  |    |
| gtaagtocag gagatago                        | 18 |
|  |    |
|  |    |
| <210: 13                                   |    |
| ₹211: 18                                   |    |
| <212: DNA                                  |    |
| <213: Artificial Sequence                  |    |
|  |    |
| ×220:                                      |    |
| <pre>%223: Antisense Oligonuclectide</pre> |    |
|  |    |
| :401: 13                                   |    |
| atttcactgt aaacggct                        | 18 |
|  |    |
|  |    |
| k310: 14                                   |    |
| 4 211 to 18                                |    |
|  |    |

. 212) INA

| <213   |    |
|--|----|
| <pre><pre><pre><pre></pre></pre></pre></pre> |    |
| CD3% Antisense Cligonuslectife               |    |
| 14008-14                                     |    |
| gottgaagaa atgittita                         | 13 |
|  |    |
| <pre>%210:0 15</pre>                         |    |
| <pre>&lt;211&gt; 18</pre>                    |    |
| :010 >                                       |    |
| k113% Artificial Sequence                    |    |
|  |    |
| :220:-                                       |    |
| (223> Antisense Oligonucleotide              |    |
|  |    |
| 4:400:- 15                                   |    |
| ggotgotgag aatotgaa                          | 18 |
|  |    |
|  |    |
| <pre></pre>                                  |    |
|  |    |
| (213) Artificial Sequence                    |    |
|  |    |
| :220:-                                       |    |
| <223> Antisense Oligonucleotide              |    |
|  |    |
| <400> 16                                     |    |
| gitcattcca ttcagttg                          | 18 |
|  |    |
|  |    |
| *210. 17                                     |    |
| <211) 13                                     |    |
| <212 / INA                                   |    |
| +2132 Artificial Sequence                    |    |
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| <pre>&lt;223: Antisense Sligenusleotide</pre>    |     |
|--|-----|
| RADOL GT   |     |
| agtaggtttt ggtggttt                              | 1.5 |
|  |     |
|  |     |
| RDIDW 18   |     |
|  |     |
| H212: DNA  |     |
| 0:213: Artificial Sequence                       |     |
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| 0.223 - Antisense Oligonucleotide                |     |
| :400: 15   |     |
| ttatteatae egitgitg                              | 18  |
| ,eacteded egoegoeg                               |     |
|  |     |
| <210> 19   |     |
| :211:- 18  |     |
| <212: DNA  |     |
| 213. Artificial Sequence                         |     |
|  |     |
| :220:  |     |
| <pre>&lt;223&gt; Antisense Oligonucleotide</pre> |     |
|  |     |
| :400:- 19  | 18  |
| atteageatt tigtaagg                              | 10  |
|  |     |
| :210:- 00  |     |
| <211: 16   |     |
| <212 - ENA                                       |     |
| <213> Artificial Sequence                        |     |
|  |     |
| 4.020.   |     |
| -Cl3/ Antisense Cligonucleotide                  |     |
|  |     |
| 4.00 2.  |     |

| addadāgāad tīgāāggītt                      | 18 |
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| <pre>&lt;010&gt; 01</pre>                  |    |
| <pre>&lt;211&gt; 16</pre>                  |    |
| <010 % INA                                 |    |
| <pre>&lt;213&gt; Artificial Sequence</pre> |    |
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| 4.000;                                     |    |
| ROD3: Antisense Oligomuoleotide            |    |
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| 4400% C1                                   |    |
| atttootggg atgtgogg                        | 18 |
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|  |    |
| H210H 12                                   |    |
| K211: 18                                   |    |
| <210: DNA                                  |    |
| <213: Artificial Sequence                  |    |
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| :(220):                                    |    |
| R223: Antisense Oligonucleptide            |    |
|  |    |
| k400: 22                                   |    |
| obgetettgg gtetggea                        | 18 |
|  |    |
|  |    |
| <210: 23                                   |    |
| <211: 18                                   |    |
| :212: ENA                                  |    |
| k213. Artificial Sequence                  |    |
|  |    |
| < 200 -                                    |    |
| <223: Antisense Oligonucleotide            |    |
|  |    |
| <400% 23                                   |    |
| uttereating controlog                      | 18 |

| 62703 74   |    |
|--|----|
| 4211: 18   |    |
| 4212: INA  |    |
| %213% Artificial Sequence                        |    |
|  |    |
| 4220 h   |    |
| <pre>&lt;223&gt; Antisense Oligonuoleotide</pre> |    |
|  |    |
|  |    |
| atoptitigia titotito                             | 18 |
|  |    |
|  |    |
| k210× 25   |    |
| <211> 18   |    |
| 3212> DNA  |    |
| <213> Artificial Sequence                        |    |
|  |    |
| :2202  |    |
| 32232 Antisense Oligonucleotide                  |    |
|  |    |
| ま4002 25   |    |
| tidaagtott ottocaat                              | 18 |
|  |    |
|  |    |
| -:210> 26  |    |
| <211> 18   |    |
| H212H DNA  |    |
| :213: Artificial Sequence                        |    |
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| $\pm 223 	imes$                                  |    |
| :223: Antisense Oligonusleotide                  |    |
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| 4400; 26   |    |
| attggtotot ogtottto                              | 18 |
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| 4210 × 17  |    |
| Control in a                                     |    |

:Ž11: INA

| Rolls & Affilistal Sequence              |    |
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| R400: 17                                 |    |
| pdaadttott ttgoogaa                      | 1ê |
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| (D10) AS                                 |    |
| .010. 18                                 |    |
| CLID - INA                               |    |
| :213: Artificial Sequence                |    |
| :220:                                    |    |
| ::223: Antisense Oligonucleotide         |    |
|  |    |
| 4400× 28                                 |    |
| utgenessee actegite                      | 18 |
|  |    |
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| R210x 29                                 |    |
| <211> 18                                 |    |
| :212> DNA                                |    |
| :213: Artificial Sequence                |    |
| k(200:                                   |    |
| 3220.<br>32232 Antisense Oligonuclectide |    |
| - Azig, Americanse origonaciectus        |    |
| -:400:- 29                               |    |
| gtottcagtg ttttcatt                      | 18 |
|  |    |
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| <2109 30                                 |    |
| <211 / 18                                |    |
| K212W LWA                                |    |
| <2135 Artificial Sequence                |    |
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| £200>                                    |    |

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| Serede esta de   | 1.5 |
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| <pre>&lt;210&gt; 31</pre>  |     |
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| -(312)- DNA  |     |
| x213 - Artificial Sequence   |     |
|  |     |
| .000%  |     |
| .313 - Antisense Cligonuclectide   |     |
|  |     |
| <400 > 31  | 18  |
| botgtttact geteteec  | 10  |
|  |     |
| 0:210:- 32   |     |
| <211: 18   |     |
| kD11> DNA  |     |
| <pre>&lt;213&gt; Artificial Sequence</pre>   |     |
|  |     |
| 4220p  |     |
| <221> Antisense Oligonucleotide  |     |
|  |     |
| -:400:- 32   |     |
| ocachactad agageagg  | 18  |
|  |     |
| <210 × 33  |     |
| <pre></pre>  |     |
| <212 > LNA   |     |
| <213: Artificial Sequence  |     |
| -  |     |
| <220>  |     |
| k2232 Antisense Oligonuoleotide  |     |
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| obbt/stbg/bagtasas               | <b>.</b> 5 |
|----------------------------------|------------|
|                                  |            |
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| <210 34                          |            |
| X211 16                          |            |
| <pre>&lt;010 + INA</pre>         |            |
| kD13 Artificial Sequence         |            |
|                                  |            |
| <220%                            |            |
| <223 - Antisense Oligonucleotide |            |
|                                  |            |
| :400:- 34                        |            |
| aaagnoatag odagtigo              | 18         |
|                                  |            |
|                                  |            |
| <210: 35                         |            |
| -:211: 18                        |            |
| :212: DNA                        |            |
| -:213: Artificial Sequence       |            |
|                                  |            |
| e(220)                           |            |
| +223: Antisense Oligonuclectide  |            |
|                                  |            |
| :400: 35                         |            |
| acattgaggg agtcgttg              | 18         |
|                                  |            |
|                                  |            |
| <:210:- 36                       |            |
| <211: 18                         |            |
| <212: DNA                        |            |
| <213: Artificial Sequence        |            |
|                                  |            |
| <200:                            |            |
| <223: Antisēnse Oligonucleotide  |            |
|                                  |            |
| <400: 36                         |            |
| goodttigot ttooagag              | 18         |
|                                  |            |

| NOTE A STORE OF THE STORE OF TH |    |
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| <pre>&lt;2119 18</pre>   |    |
| k212a IMA  |    |
| «213» Artificial Sequence  |    |
|  |    |
| K200%  |    |
| K223% Antisense Oligonuoleotide  |    |
|  |    |
| 4400: 37   |    |
| ltoagaotgg agaggago  | 18 |
|  |    |
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| w21) + 38  |    |
| :211   |    |
| .212 - DNA   |    |
| 32135 Artificial Sequence  |    |
| :1.23  |    |
| <pre>%223 Antisense Oligonucleotide</pre>  |    |
|  |    |
|  |    |
| 4400 × 38  |    |
| 4400:- 38<br>aaagaaggga taagcact   | 18 |
|  | 18 |
|  | 18 |
|  | 18 |
| aaagaaggga taagcact <210: 39 <211: 18  | 18 |
| ARAGRAGGA taagcact  <210: 35  <211: 18  <212> DNA  | 18 |
| aaagaaggga taagcact <210: 39 <211: 18  | 18 |
| <pre>48agaaggga taagcact  &lt;210: 39  &lt;211: 18  &lt;212&gt; DNA  &lt;213&gt; Artificial Sequence</pre>   | 18 |
| <pre> «210: 35 «211: 18 «212&gt; DNA «213&gt; Artificial Sequence </pre>   | 18 |
| <pre>48agaaggga taagcact  &lt;210: 39  &lt;211: 18  &lt;212&gt; DNA  &lt;213&gt; Artificial Sequence</pre>   | 18 |
| <pre>aaagaagga taagcact  &lt;110: 35 &lt;111: 18 &lt;112&gt; DNA &lt;113&gt; Artificial Sequence  &lt;120&gt; &lt;1213: Antisense Oligonucleotide</pre>  | 18 |
| <pre>48agaaggga taagcact  &lt;210: 39 &lt;211: 18 &lt;212: DNA &lt;213: Artificial Sequence  &lt;220: &lt;223: Antisense Oligonucleotide  &lt;400: 39</pre>  |    |
| <pre>aaagaagga taagcact  &lt;110: 35 &lt;111: 18 &lt;112&gt; DNA &lt;113&gt; Artificial Sequence  &lt;120&gt; &lt;1213: Antisense Oligonucleotide</pre>  | 18 |
| <pre>48agaaggga taagcact  &lt;210: 39 &lt;211: 18 &lt;212: DNA &lt;213: Artificial Sequence  &lt;220: &lt;223: Antisense Oligonucleotide  &lt;400: 39</pre>  |    |
| <pre>aaagaagga taagcact  4210: 35  4211: 18  4212: DNA  4213: Artificial Sequence  4220: 4223: Antisense Oligonucleotide  4400: 39  6tgeetetet eteeteeg</pre>  |    |
| <pre>48agaaggga taagcact  &lt;210: 39 &lt;211: 18 &lt;212: DNA &lt;213: Artificial Sequence  &lt;220: &lt;223: Antisense Oligonucleotide  &lt;400: 39</pre>  |    |

| - EEST MESEES AND GOOGLOO                  |     |
|--|-----|
| k200°                                      |     |
| .123 Antisense Cligonucleotide             |     |
|  |     |
| .400%_40                                   |     |
| praggetaaa deaggetg                        | 2.8 |
|  |     |
|  |     |
| R210: 41                                   |     |
| k211k-18                                   |     |
| :212: DNA                                  |     |
| :213: Artificial Sequence                  |     |
|  |     |
| <223:                                      |     |
| <22}> Antisense Oligonucleotide            |     |
|  |     |
| $400 \times 40$                            | 1.0 |
| tgtotgggto cacegtge                        | 18  |
|  |     |
| +:210: 42                                  |     |
| :211: 18                                   |     |
| <212 DNA                                   |     |
| (213) Artificial Sequence                  |     |
|  |     |
| :220:                                      |     |
| <223 - Antisense Oligonucleotide           |     |
|  |     |
| 84005 42                                   |     |
| gaogtgoott totgotad                        | 18  |
|  |     |
|  |     |
| :2101 43                                   |     |
| :211: 18                                   |     |
| 2212 <sub>8</sub> UNA                      |     |
| <pre>&lt;013&gt; Artificial Sequence</pre> |     |
|  |     |

| 4223/ Antisense Cligonuclectide   |     |
|---|-----|
| ka.0% 43  |     |
| attotocoaa agogtoco   | 1.5 |
|   |     |
|   |     |
| 4210: 44  |     |
| R211: 18  |     |
| RDIG: DNA   |     |
| 00213: Artificial Sequence  |     |
|   |     |
| <pre>&lt;220:</pre>   |     |
| .223: Antisense Cligonucleotide   |     |
|   |     |
| - (400)의 실실<br>   | 18  |
| totggoadt ttotatga  | 10  |
|   |     |
| <210x 45  |     |
| :211> 18  |     |
| RECEIVE DNA   |     |
| d213> Artificial Sequence   |     |
|   |     |
| %220x   |     |
| <pre>&lt;22}&gt; Antisense Oligonucleotide</pre>  |     |
|   |     |
| ⟨400⟩ 45  |     |
| cottoagoaa aacaaaac   | 18  |
|   |     |
| <210x 46  |     |
| :211> 18  |     |
| <212> ENA   |     |
| <213> Artificial Sequence   |     |
| -   |     |
| ×226>   |     |
| <pre><pre><pre><pre><pre></pre></pre></pre><pre></pre></pre><pre></pre></pre> <pre></pre> |     |
|   |     |
| 44009 46  |     |

aactgasata acaactta

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-11. 47 40114 IB 1010 - DNA %213% Artificial Sequence :220:2 :323: Antisense Oliganualeatide .4000 47 18 ccaacaaaac agtocaaa :210> 48 <211> 3454 <212: DNA <213: Mus musculus</p> <220: :221: CDS :222: +575)...(2749) :400> 48 ggeaegagee gagttggagg aageagegge ageggeageg geageggtag eggtgaggae 60 ggotgtgcag ccaaggaace gggacagega agegacggea ggtcgcaget ggatcgcagg 120 agostgggag stgggagstt sagaggddgo tgaagsddag gstgggsaga ggaaggaago 180 gagoogacoo ggaggtgaag otgagagtgg agogtggcag taaaatcaga ogacagatgg 240 abagtigtigab aggaabgtisa gagaggattig ggbbtigbtig ogagagtbag bottggagtba 300 aggtgttgas aagttgotga gaaggacacg tgggaggacg gtggcgsgsg gagggagags 360 potytottoa ytoaccopyt tyatyyayya dayatyyaba ybayboyyab yyddaytdab 420 ototottaaa ootitiggata giggiootiti gigotoigoi ggacacoigi iggggattii 480 ageopation ongaabload tittotottaa aabghaaach oggaoggoag tigtigigagoo 540 agetretetg tggeagggea stagagetge agas atg agt gea gag gge tas cag 595 Met Ser Ala Glu Gly Tyr Gln -5

tad aga goa otg tad gad tad aag aag gag oga gag gaa gad att gad - 643 Tyr Arg Ala Leu Tyr Asp Tyr Lys Lys Slu Arg Slu Slu Asp Ile Asp 10 25

|            |            | Cac   | stg         | 999   | 393   | ata        | ot g  | art     | gtg      | RAT  | AAA  | 330  | 133              | tta   | j: 9       | gja    | €91  |
|------------|------------|-------|-------------|-------|-------|------------|-------|---------|----------|------|------|------|------------------|-------|------------|--------|------|
|            | <u>-</u> ∵ | His   | Leu         | зіу   | Asp   | Tle        | Leu   | Thy     | ∵al      | Asi. | Lys  | 317  | Ser              | Leu   | Wal        | Ala    |      |
|            |            | 2.5   |             |       |       |            | 3.0   |         |          |      |      | 3 5  |                  |       |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            | tgg    | -35  |
| L          | eu         | Gly   | Phe         | Ser   | Asp   | Gly        | Gln   | Glu     | Ala      | Arg  | Pro  | Glu  | Asp              | Ile   | Gly        |        |      |
| -          | <b>1</b> 0 |       |             |       |       | <b>÷</b> 5 |       |         |          |      | 50   |      |                  |       |            | 55     |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       | cca        |        | 787  |
| L          | ≘u         | Asn   | Gly.        | Tyr   |       | Glu        | Thr   | +11.17  | 'ڏِ ۽ في |      | Arg  | Gir  | ASD              | Nitre | Pro        | ्रें इ |      |
|            |            |       |             |       | 60    |            |       |         |          | 6.5  |      |      |                  |       | 70         |        |      |
| 2          | ~+         | + = 0 | ~++         | 722   | tar   | a + +      | മവം   | ann     | .a .a .a | 3013 | a++  | - ca |                  | ,~,~+ | act        | aaa    | 835  |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       | Thr        |        |      |
|            |            |       | V           | 75    |       |            | 0.4.3 | 5       | 80       | 5    |      |      |                  | 3.5   |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
| a.         | aq         | cct   | <b>0</b> 99 | 000   | aat   | oga        | add   | att     | aat      | gtt  | gat  | cog  | ggt              | tot   | tca        | aaa    | 883  |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       | Ser        |        |      |
|            |            |       | 90          |       |       |            |       | 95      |          |      |      |      | 100              |       |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
| a.         | Ξŧ         | gaa   | gat         | gac   | acg   | gag        | cag   | caa     | geg      | ttg  | ccc  | ctt  | cct              | gar   | ctg        | gcc    | 931  |
| T          | nr         | Glu   | Ala         | Asp   | Thr   | Glu        | Gln   | Gln     | Ala      | Leu  | Pro  | Leu  | Pro              | Asp   | Leu        | Ala    |      |
|            |            | 105   |             |       |       |            | 110   |         |          |      |      | 115  |                  |       |            |        |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
| -          | -          |       |             |       |       |            |       |         |          |      |      |      |                  |       | aag        |        | 979  |
| G          | lu         | Gln   | Phe         | Ala   | Pro   | Pro        | Asp   | Val     | Ala      | Pro  |      | Leu  | Leu              | Ile   | Lys        |        |      |
| 1          | 20         |       |             |       |       | 125        |       |         |          |      | 130  |      |                  |       |            | 135    |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        | 1007 |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       | tac        |        | 1027 |
| 1          | eu         | 3 102 | Aia         | ile   | 7 1 0 | Lys        | Lys   | '' نہ ف |          | 145  | Ey's | ser  | 1111             | Ten   | Tyr<br>150 | wid    |      |
|            |            |       |             |       | _4 i  |            |       |         |          | 740  |      |      |                  |       | 100        |        |      |
| 5          | 0.5        |       | 2 70        | + ~ ~ | 270   | 220        |       | 703     | caa      |      | ana  | cad  | ~ <del>-</del> - | a++   | gar        | tar    | 1075 |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            | Cys    |      |
| *          |            | O =   |             | 155   |       | 11011      |       |         | 160      |      | 3    |      |                  | 165   |            | - • -  |      |
|            |            |       |             |       |       |            |       |         |          |      |      |      |                  |       |            |        |      |
| <b>3</b> . | аt         | qos   | gea         | toa   | qta   | gac        | tta   | gau     | atg      | ato  | gar  | gta  | cac              | gto   | tta        | gca    | 1123 |
| -          |            | _     |             |       |       | 3          |       | -       |          |      |      |      |                  |       |            |        |      |

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| ca 1507<br>rc                        |
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| ttg    | cag   | gat   | gat     | EEĘ   | tgg   | t a c            | :93    | gga   | gac  | ato   | tsa  | agg          | ĒĒĘ   | даа   | gig   | 1603 |
|--------|-------|-------|---------|-------|-------|------------------|--------|-------|------|-------|------|--------------|-------|-------|-------|------|
| Leu    | 31m   | Asp   | Ala     | 314   | Trp   | Tyr              | Trp    | gly   | Asp  | Πė    | Ser  | Arg          | 314   | 314   | Val   |      |
|        |       | 3 3 3 |         |       |       |                  | 3 3 5  |       |      |       |      | 340          |       |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| 5 3 t  | ~ = = | ааа   | ~+ ¬    | 2013  | ner.  | 3 ~ <del>-</del> | 3~*    | a a t | aaa  | 3 7.7 |      | tta          | ata   | caa   | gas   | 1651 |
|        |       | Lys   |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| ASI.   |       | -,5   | _ U     | AT 9  | Mar   |                  | A.a.   | Mar   | 3-1  |       | 355  |              |       | -11-9 |       |      |
|        | 345   |       |         |       |       | 3 5 3            |        |       |      |       | 355  |              |       |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
|        |       | act   |         |       |       |                  |        |       |      |       |      |              |       |       |       | 1699 |
| Ala    | Ser   | Thr   | Lys     | Met   | His   | 3lÿ              | Asp    | Tyr   | Thr  | Leu   | Thr  | Pro          | Arg   | Lys   | Gly   |      |
| 360    |       |       |         |       | 365   |                  |        |       |      | 3 7 0 |      |              |       |       | 375   |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| gga    | aat   | aac   | aaa     | tta   | atc   | aaa              | atc    | ttt   | cac  | cgt   | gat  | gga          | aaa   | tat   | aac   | 1747 |
| Gly    | Asn   | Asn   | Lys     | Leu   | Ile   | Lys              | Ile    | Phe   | His  | Arg   | Asp  | ${\rm Gl}_Y$ | Lys   | Tyr   | Gly   |      |
|        |       |       |         | 380   |       |                  |        |       | 385  |       |      |              |       | 390   |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| tta    | tot   | gat   | сва     | tta   | acc   | tta              | aac    | tat   | gtg  | gtt   | gag  | tta          | ata   | aac   | cac   | 1795 |
|        |       | Asp   |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
|        |       | _     | 3 9 5   |       |       |                  |        | 400   |      |       |      |              | 405   |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| ± 0.7  | 777   | aat   | ~~~     | +.~+  | + + s | ac+              |        | tac   | 227  | 000   | aad  | a-a          | gat   | a+a   | aad   | 1843 |
|        |       | Asn   |         |       |       |                  |        |       |      |       |      |              |       |       |       | 10.0 |
| 1 M.E. | arg   |       | لمالداف | 561   | пел   | Aid              |        | - y - | A5.1 | PIU   | uy s |              | Asp   | va.   | د ړ د |      |
|        |       | 410   |         |       |       |                  | 415    |       |      |       |      | 420          |       |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
|        |       | tac   |         |       |       |                  |        |       |      |       |      |              |       |       | _     | 1891 |
| Leu    | Leu   | Tyr   | Pro     | Val   | Ser   | Lys              | ΤγΥ    | Gln   | Gln  | Asp   | Gln  | Val          | Val   | Lys   | Glu   |      |
|        | 425   |       |         |       |       | 430              |        |       |      |       | 435  |              |       |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| gat    | aat   | att   | gaa     | get   | gta   | 999              | aaa    | aaa   | tta  | cat   | gaa  | tat          | aat   | act   | caa   | 1939 |
| Asp    | Asn   | Ile   | Glu     | Ala   | Val   | Gly              | Lys    | Lys   | Leu  | His   | Glu  | Tyr          | Asn   | Thr   | Gln   |      |
| 440    |       |       |         |       | 445   |                  |        |       |      | 450   |      |              |       |       | 455   |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
| ttt    | saa   | gaa   | ааа     | aqt   | cqa   | gaa              | tat    | gat   | aga  | tta   | tat  | gag          | gag   | tac   | acc   | 1987 |
|        |       | Glu   |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |
|        |       |       | -1-     | 460   |       |                  | 4 =    | - 1   | 465  |       | •    |              |       | 470   |       |      |
|        |       |       |         | 100   |       |                  |        |       |      |       |      |              |       |       |       |      |
| ~~+    | 3.05  | tcc   | 75.7    | ~ a a | a+ 0  | 000              | a + -+ | 222   | ara  | 200   | ~-+  | a+ ~         | gaa   | ara   |       | 2035 |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       | 2000 |
| arg    | inr   | Ser   |         | نايي  | i_e   | J.E              | .∙.et  |       | Arg  | 1111  | n.a  | E            |       | A.a   | FE    |      |
|        |       |       | 475     |       |       |                  |        | 480   |      |       |      |              | 4 6 5 |       |       |      |
|        |       |       |         |       |       |                  |        |       |      |       |      |              |       |       |       |      |

|     |     | асс    |      |            |       |      |     |     |     |      |              |     |     |     |          | 2 1 é 3 |
|-----|-----|--------|------|------------|-------|------|-----|-----|-----|------|--------------|-----|-----|-----|----------|---------|
| Asn | 31  | Thr    | īļē  | Lys        | īlė   | Fhe  | 314 | 314 | Glm | J.:s | 3ln          | Thr | 3lm | 31u | Arg      |         |
|     |     | igar C |      |            |       |      | 495 |     |     |      |              | 500 |     |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
| tac | agc | ааа    | gaa  | tac        | ata   | gag  | аад | ttt | aaa | ege  | gaa          | ggc | зас | gag | aaa      | 2131    |
| Tyr | Ser | Lys    | Glu  | Tyr        | Ile   | Glu  | Lys | Phe | Lys | Arg  | 3lu          | Gly | Asn | Glu | Lys      |         |
|     | 505 |        |      |            |       | 510  |     |     |     |      | 515          |     |     |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
| gaa | att | caa    | agg  | att        | atg   | cat  | aac | cat | gat | gss  | ctg          | aag | tag | cgt | ato      | 2179    |
| 31. | Ile | Gln    | Arg  | Ile        | Met   | His  | Asn | His | Asp | lys  | Leu          | Lys | Ser | Arg | Ile      |         |
| 520 |     |        |      |            | 525   |      |     |     |     | 530  |              |     |     |     | 535      |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
| agt | gag | atc    | att  | gac        | agt   | agg  | agg | agg | ttg | gaa  | gaa          | gac | ttg | aag | аад      | 2227    |
| Ser | Glu | Ile    | Ile  | Asp        | Ser   | Arg  | Arg | Arg | Leu | Glu  | Glu          | Asp | Leu | Lys | Γλε      |         |
|     |     |        |      | 540        |       |      |     |     | 545 |      |              |     |     | 550 |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
| сад | gca | get    | gag  | tac        | cga   | gag  | atc | gac | aaa | cgc  | atg          | зас | agt | att | аад      | 2:275   |
| Gln | Ala | Ala    | Glu  | Tyr        | Arg   | Glu  | Ile | Asp | Lys | Arg  | Met          | Asn | Ser | Ile | Lys      |         |
|     |     |        | 555  |            |       |      |     | 560 |     |      |              |     | 565 |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
| 203 | дас | St S   | atc  | cag        | ttg   | aga  | aag | aca | aga | gac  | caa          | tac | ttg | atg | tgg      | 2/3/2/3 |
| Pro | Asp | Leu    | Ile  | Gln        | Leu   | Arg  | Lys | Thr | Arg | Asp  | 31n          | Tyr | Leu | Met | Trp      |         |
|     |     | 570    |      |            |       |      | 575 |     |     |      |              | 580 |     |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     | 999      | 2371    |
| le. |     | Gln    | Lys  | Gly        | Val   |      | Glņ | Lys | Lys | Leu  |              | Glu | Trp | Leu | Gly      |         |
|     | 585 |        |      |            |       | 590  |     |     |     |      | 595          |     |     |     |          |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          |         |
|     |     | aat    |      |            |       |      |     |     |     |      |              |     |     |     |          | 2419    |
|     | Glu | Asn    |      |            |       | Gln  | Tyr | Ser |     |      | Blu          | Asp | Asp | Glu |          |         |
| 600 |     |        |      |            | 605   |      |     |     |     | 51)  |              |     |     |     | 615      |         |
|     |     |        |      |            |       |      |     |     |     |      |              |     |     |     |          | 0       |
| _   |     |        |      |            |       |      |     |     |     |      |              |     |     |     | cga<br>- | 2467    |
| Leu | T   | His    | H- C | Z.cr.      | 17:11 | Lys  | Thr | Trp | Asn | ∵al  | $G_{\perp}y$ | Ser | Ser | Asn | Arg      |         |
|     | PIC |        |      |            |       | •    |     |     |     |      |              |     |     |     |          |         |
|     | PIC |        |      | 620        | 324   | •    |     |     | 625 |      |              |     |     | 630 |          |         |
|     |     |        |      | 620        |       |      |     |     |     |      |              |     |     |     |          | 0515    |
|     | aaa |        | gag  | 620<br>aac | cta   | t 19 | oga |     | aag |      |              |     |     | tta | att      | 2515    |

| 645 645 |
|---------|
|---------|

| gto ogg gag ago agt aag cag ggo tgo tat goo tgo too gta g     | tg gta         |
|---|----------------|
| Val Arģ Glu Ser Ser Lys Gln Gly Cys Tyr Ala Cys Ser Val V     | al Val         |
| 650 655 660   |                |
|   |                |
| gae gge gaa gto aag cat tgo gto att aas aag act goo aco g     | ggo tat 1611   |
| Asp Gly Glu Val Lys His Cys Val Ile Asn Lys Tor Ala Thr G     | Sly Tyr        |
| 665 670 675   |                |
|   |                |
| ggo tit geo gag occ tad aan dig tad ago too oig aag gag o     | etg gtg 2659   |
| Gly Phe Ala Glu Pro Tyr Ash Leu Tyr Ser Ser Leu Lys Glu L     | Leu Val        |
|   | 695            |
|   |                |
| ota dat tat daa dad add too dto gtg dag dad aat gad too d     | oto aat 1707   |
| Let His Tyr Gln His Thr Ser Let Val Gln His Asn Asp Ser L     |                |
| -   | 710            |
|   |                |
| gto aca ota goa tao ooa gta tat goa caa cag agg oga tga       | 2749           |
| Val Thr Leu Ala Tyr Pro Val Tyr Ala Gln Gln Arg Arg *         |                |
| 715 720   |                |
|   |                |
| agogotgooo toggatooag ttootoacet toaageeace caaggeetet ga     | agaagcaaa 2809 |
| gggotootot obagooogab otgtgaadtg agotgbagaa atgaagbogg ot     | igtotgdad 2869 |
| atgggastag agstttettg gasaaaaaga agtsggggaa gacabgsags ot     | oggadtgt 2929  |
| tggatgaeca gaegttteta aeettateet ettiittet tietttetti ot      | ittotttot 2989 |
| thousests outlottes trouttett officiality tagagorada as       |                |
| aabababaga gagaaagaaa tgbaaaaaato totoogtgba gggabaaaga gg    |                |
| - catggtgott gttaacgott totgaagott tabbagotac aagttgggab tt   |                |
| agaaggtaga dagggoogaa gagootgogo otggggoogo ttggtobago ot     |                |
| otigggtgtog otigggtgtgg tigaacccaga cacatcacac tigtggattat it |                |
| aaagagegaa tgatatgtat bagagageeg egtotgetea egeaggaeab tt     |                |
| - battgatgba gtbtgttbgg aggaaaaatg aaacaccaga aaacgttttt gt   |                |
|   |                |

<sup>&</sup>lt;210> 49

atcaagtcag caaccaacaa cccaccaaca gaaaaaaaaa aaaaa

3454

<sup>.211&</sup>gt; 21

<sup>4.212&</sup>gt; 23A

k2130 Artificial Sequence

| Section 2                                  |    |
|--|----|
| QCC3: FCR Primer                           |    |
|  |    |
|  |    |
|  | 21 |
| gogtggdagt aaaatcagad g                    |    |
|  |    |
| k210% 50                                   |    |
| .211: 20                                   |    |
| ROIDE DNA                                  |    |
| .213: Artificial Sequence                  |    |
|  |    |
| kana nik                                   |    |
| <pre>&lt;:023: PCR Primer</pre>            |    |
| - ULDS FCR FILMCI                          |    |
|  |    |
| 4400> 50                                   |    |
| -coacgigico ticicagoaa                     | 20 |
|  |    |
| k210> 51                                   |    |
| #211> 22                                   |    |
| RINE DNA                                   |    |
| %211> Artificial Sequence                  |    |
| •  |    |
| :321>                                      |    |
| ROZEV PCR Probe                            |    |
| Anziv Per Fiobe                            |    |
|  |    |
| (401) 51                                   |    |
| ngggddtogo tgogagagto ag                   | 22 |
|  |    |
| k210x 52                                   |    |
| :211: 20                                   |    |
| <212 > DNA                                 |    |
| <pre>&lt;013&gt; Artificial Sequence</pre> |    |
| 1  |    |
| <220>                                      |    |
|  |    |
| <121> Antisense Oligonucleotide            |    |
|  |    |
| <400% E2                                   |    |
| egetgettee tecaactegg                      | 20 |

egetgettee tecaactegg

| <210% E3   |    |
|--|----|
| KD114 D0   |    |
| RECENTINA  |    |
| <213% Artificial Sequence  |    |
|  |    |
| <220%  |    |
| .223: Antisense Oligonuoleotide  |    |
|  |    |
| k400x 53   |    |
| ngotocaeto teagetteas  | 20 |
|  |    |
| :210x 54<br>:211x 00   |    |
| :2128 DNA  |    |
| <pre></pre>  |    |
| Aprily Apriliated Dogucine   |    |
| :220>  |    |
| <223> Antisense Oligonucleotide  |    |
|  |    |
|  |    |
| 4400> 54   |    |
| <pre>%400&gt; 54<br/>%patetgtee tecatoaabg</pre>   | 20 |
|  | 20 |
|  | 20 |
| <pre>coatctgtcc tccatcaabg  :210&gt; 55  :211&gt; 20</pre>   | 20 |
| coatctgtcc tocatcaacg  :210> 55  :211> 20  <212> DNA   | 20 |
| <pre>coatctgtcc tccatcaabg  :210&gt; 55  :211&gt; 20</pre>   | 20 |
| contetgted todatcaacg  :210> 55  :211> 20  :212> DNA  :213> Artificial Sequence  | 20 |
| cratetytee tecatraapy  :210> 55  :211> 20  :212> DNA  :213> Artificial Sequence  | 20 |
| contetgted todatcaacg  :210> 55  :211> 20  :212> DNA  :213> Artificial Sequence  | 20 |
| <pre>contetgted tecationed  :210&gt; 55  :211&gt; 20  :212&gt; DNA  :213&gt; Artificial Sequence  :220&gt;  :223&gt; Antisense Oligonucleotide</pre>   | 20 |
| coatctgtcc tocatcaacg  :210> 55 :211> 20 :212> DNA :213> Artificial Sequence  <220> :223> Antisense Oligonucleotide  :400> 55  |    |
| <pre>contetgted tecationed  :210&gt; 55  :211&gt; 20  :212&gt; DNA  :213&gt; Artificial Sequence  :220&gt;  :223&gt; Antisense Oligonucleotide</pre>   | 20 |
| <pre>cratetgtcd todatsaapg  cpatetgtcd todats</pre> |    |
| coatctgtcc tocatcaacg  :210> 55 :211> 20 :212> DNA :213> Artificial Sequence  <220> :223> Antisense Oligonucleotide  :400> 55  |    |
| <pre>cratetgtee tecatcaapg  :210&gt; 55 :211&gt; 20 :212&gt; DNA :213&gt; Artificial Sequence  :220&gt; :223&gt; Antisense Oligonucleotide  :400&gt; 55 gractcatgt etgeagetet :210&gt; 56</pre>  |    |
| <pre>coatctgtcc tccatcaacg  clic</pre>   |    |

2220×

| kCC3 / Antisense Cligonholestide               |    |
|--|----|
| <430> 56                                       |    |
| octggccatc actgaatcca                          | 20 |
|  |    |
| <210% 87                                       |    |
| <pre>&lt;011% 00</pre>                         |    |
| 4212 DNA                                       |    |
| (113): Artificial Sequence                     |    |
|  |    |
| -:220:·  |    |
| :223: Antisense Cligonucleotide                |    |
|  |    |
| :400:- 57                                      |    |
| ocagtggttt cattgtages                          | 20 |
| +:210:- 58                                     |    |
| +:211:- 20                                     |    |
| S2125 DMA                                      |    |
| <pre>&lt;211&gt; Artificial Sequence</pre>     |    |
|  |    |
| <2.2 %   |    |
| ::221:: Antisense Oligonucleotide              |    |
|  |    |
| 44005 58                                       |    |
| ombigotgoto ogtgtbagbt                         | 20 |
|  |    |
| k210x 59                                       |    |
| <211> 20                                       |    |
| -:2128 DMA                                     |    |
| ROTE: Artificial Sequence                      |    |
|  |    |
| <pre>&lt;:223: Antisense Oligonucleotide</pre> |    |
| .225. Andibense diigonddieddide                |    |
| <400> 59                                       |    |
| totocaagto cactgacgog                          | 20 |
|  |    |

V2109 60

| 8225 20                          |    |
|----------------------------------|----|
| ×212 × DNA                       |    |
| gliše Artificial Sequence        |    |
|                                  |    |
| /g2009                           |    |
| k223 - Antisense Oligonuoleotide |    |
|                                  |    |
| N400× 60                         |    |
| noggogagat agogtttgaa            | 20 |
|                                  |    |
| - 213: 61                        |    |
| .211 / 20                        |    |
| <212> DNA                        |    |
| <213: Artificial Sequence        |    |
|                                  |    |
| <220>                            |    |
| <223> Antisense Oligonuclectide  |    |
|                                  |    |
| :4005-61                         |    |
| atactgaago gtaagccaac            | 20 |
|                                  |    |
| <217× 62                         |    |
| <2118 20                         |    |
| 0:212:0 DNA                      |    |
| <211> Artificial Sequence        |    |
|                                  |    |
| R2236                            |    |
| - 221: Antisense Oligonucleotide |    |
|                                  |    |
| <4002 62                         |    |
| tgatggtgat ggatgtatat            | 20 |
|                                  |    |
| <210 / 63                        |    |
| <211× 20                         |    |
| <212 - DNA                       |    |
| <213: Artificial Sequence        |    |
|                                  |    |
| 1×2004                           |    |
| 113% Antisense Sligonuclestide   |    |

| K4005 60   |    |
|--|----|
| ggtgtaagag tgtaätogoo                            | 20 |
|  |    |
| <pre><pre><pre>&lt; pre&gt;</pre></pre></pre>    |    |
| K2119-20   |    |
| Raidy DNA  |    |
| k213: Artificial Sequence                        |    |
|  |    |
| K2D014   |    |
| 2003: Antisense Oligonucleotide                  |    |
|  |    |
| k400% 64   |    |
| optgotggta tittggacapt                           | 20 |
|  |    |
| <210> 65   |    |
| <pre>&lt;211&gt; 20</pre>                        |    |
| dl12 > DNA                                       |    |
| HIII Artificial Sequence                         |    |
|  |    |
| k120>  |    |
| <pre>&lt;123&gt; Antisense Oligonucleotide</pre> |    |
|  |    |
| -:400× 65  |    |
| gutdetgggt tiggeattgt                            | 20 |
|  |    |
| :210% 66<br>::211:2 20                           |    |
| <212× ENA  |    |
| <pre>&lt;2139 Artificial Sequence</pre>          |    |
| Allis Altificial Sequence                        |    |
| HI2269   |    |
| <pre>%223&gt; Antisense Oligonucleotide</pre>    |    |
|  |    |
| -:400:- 66                                       |    |
| ogatototog gtactcagot                            | 20 |
|  |    |
| k210x 67   |    |
| <211> 20   |    |
| 4212   |    |

| %೬೨೨ ಕ    | ntilicial Sequence   |     |
|-----------|--|-----|
| <220 ·    |  |     |
| ₹223÷ A   | untisense Cligonuoleotide  |     |
| :433 · €  |  |     |
| getekeg   | ada tiddadgidi 2   | ~   |
| k2105 6   |  |     |
| 42115 C   |  |     |
| 42125 D   |  |     |
|           | artificial Sequence  |     |
|           | - Ellistat Begaense  |     |
| < 220:    |  |     |
| 223:- A   | antisense Oligonucleotide  |     |
|           |  |     |
| <400: 6   | ; a  |     |
| ocatage   | eegg tggeagtett 2  | : C |
|           |  |     |
| <2105 6   | 59   |     |
| <211> 2   | 0  |     |
| ::212:- D | DNA CONTRACTOR OF THE CONTRACT |     |
| edile: A  | Artificial Sequence  |     |
|           |  |     |
| <2200     |  |     |
| <22∃> A   | intisense Oligonucleotide  |     |
|           |  |     |
| <400÷ 6   |  |     |
| tttgatt   | coto agaggoottg 2  | 0 : |
|           |  |     |
| 1210:- 7  |  |     |
| <211. 2   |  |     |
| <212> D   |  |     |
| <213 ≥ A  | Artificial Sequence  |     |
| :220 -    |  |     |
|           | antisense Oligonucleotide  |     |
|           | melbenbe oligonacieotiae   |     |

<4002 T0

| ggtotobaaa gtoboaaott           | 4 %<br>v |
|---------------------------------|----------|
| kolox 71                        |          |
| K011× 20                        |          |
| 42125 CNA                       |          |
| K213: Artificial Sequence       |          |
|                                 |          |
| ×220;                           |          |
| .223: Antisense Oligonucleotide |          |
|                                 |          |
| .400> 71                        |          |
| grorgggrro accacacca            | 20       |
|                                 |          |
| H210: 72                        |          |
| <211× 20                        |          |
| <212: DNA                       |          |
| <213: Artificial Sequence       |          |
|                                 |          |
| <220×                           |          |
| <223> Antisense Oligonucleotide |          |
|                                 |          |
| 4400x 72                        |          |
| geathaatgt tototoaaag           | 20       |
|                                 |          |
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| 4211: 20                        |          |
| <212> DNA                       |          |
| <213% Artificial Sequence       |          |
|                                 |          |
| <220%                           |          |
| <223: Antisense Oligonucleotide |          |
| 166 83                          |          |
| <400:- 73                       | 20       |
| gedacegoet atgrettete           | 20       |